

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents *will not* correct images,
Please do not report the images to the
Image Problem Mailbox.

PCT

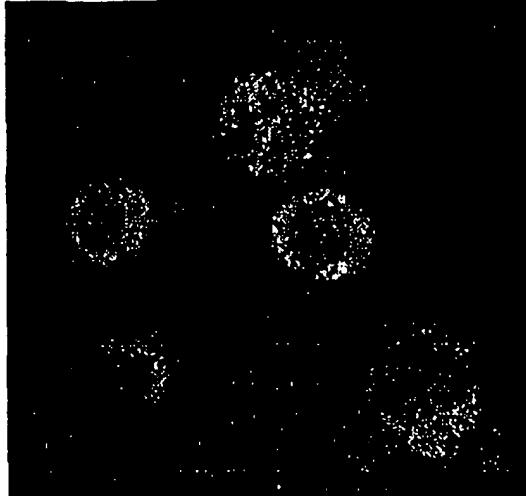
WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : A61K 9/127, C12N 15/11	A3	(11) International Publication Number: WO 97/07784 (43) International Publication Date: 6 March 1997 (06.03.97)
(21) International Application Number: PCT/US96/14146		(81) Designated States: AL, AM, AT, AU, BB, BG, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).
(22) International Filing Date: 26 August 1996 (26.08.96)		
(30) Priority Data: 08/520,385 29 August 1995 (29.08.95) US		
(71) Applicant: BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM [US/US]; 201 West 7th Street, Austin, TX 78701 (US).		
(72) Inventors: LOPEZ-BERESTEIN, Gabriel; 5630 Rutherford, Houston, TX 77096 (US). TARI, Ana, Maria; 16 Charleston Park Drive #1703, Houston, TX 77025 (US).		
(74) Agent: GOODMAN, Kenneth, D.; Arnold, White & Durkee, P.O. Box 4433, Houston, TX 77210 (US).		(88) Date of publication of the international search report: 24 April 1997 (24.04.97)

(54) Title: **LIPOSOMAL PHOSPHODIESTER, PHOSPHOROTHIOATE, AND p-ETHOXY OLIGONUCLEOTIDES**



(57) Abstract

An improved delivery system for antisense oligonucleotides involves a liposomal composition, comprising a liposome which consists essentially of neutral phospholipids and an antisense oligonucleotide that is entrapped in the liposome and is selected from the group consisting of phosphodiester oligonucleotides, phosphorothioate oligonucleotides, and p-ethoxy oligonucleotides.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AM	Armenia	GB	United Kingdom	MW	Malawi
AT	Austria	GE	Georgia	MX	Mexico
AU	Australia	GN	Guinea	NE	Niger
BB	Barbados	GR	Greece	NL	Netherlands
BE	Belgium	HU	Hungary	NO	Norway
BF	Burkina Faso	IE	Ireland	NZ	New Zealand
BG	Bulgaria	IT	Italy	PL	Poland
BJ	Benin	JP	Japan	PT	Portugal
BR	Brazil	KE	Kenya	RO	Romania
BY	Belarus	KG	Kyrgyzstan	RU	Russian Federation
CA	Canada	KP	Democratic People's Republic of Korea	SD	Sudan
CF	Central African Republic	KR	Republic of Korea	SE	Sweden
CG	Congo	KZ	Kazakhstan	SG	Singapore
CH	Switzerland	LJ	Liechtenstein	SI	Slovenia
CI	Côte d'Ivoire	LK	Sri Lanka	SK	Slovakia
CM	Cameroon	LR	Liberia	SN	Senegal
CN	China	LT	Lithuania	SZ	Swaziland
CS	Czechoslovakia	LU	Luxembourg	TD	Chad
CZ	Czech Republic	LV	Latvia	TG	Togo
DE	Germany	MC	Monaco	TJ	Tajikistan
DK	Denmark	MD	Republic of Moldova	TT	Trinidad and Tobago
EE	Estonia	MG	Madagascar	UA	Ukraine
ES	Spain	ML	Mali	UG	Uganda
FI	Finland	MN	Mongolia	US	United States of America
FR	France	MR	Mauritania	UZ	Uzbekistan
GA	Gabon			VN	Viet Nam

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 96/14146

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K9/127 C12N15/11

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DE 41 10 085 A (BOEHRINGER INGELHEIM INTERNATIONAL GMBH) 1 October 1992 see page 2, line 65 - page 3, line 20 see page 23, line 37 - line 48 ---	1,2
Y	WO 95 03788 A (BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM) 9 February 1995 see page 8, line 8 - page 11, line 31 ---	1-4,6, 10-12 -/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- 'A' document defining the general state of the art which is not considered to be of particular relevance
- 'E' earlier document but published on or after the international filing date
- 'L' document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- 'O' document referring to an oral disclosure, use, exhibition or other means
- 'P' document published prior to the international filing date but later than the priority date claimed

'T' later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

'X' document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

'Y' document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

'&' document member of the same patent family.

1

Date of the actual completion of the international search

Date of mailing of the international search report

10 March 1997

14.03.97

Name and mailing address of the ISA
European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 cpo nl.
Fax (+31-70) 340-3016

Authorized officer

Benz, K

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 96/14146

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>NUCLEIC ACIDS RESEARCH, vol. 19, no. 20, 25 October 1991, EYNSHAM , OXFORD (GB), pages 5551-5559, XP002027215</p> <p>S. AKHTAR ET AL.: "interactions of antisense DNA oligonucleotide analogs with phospholipid membranes (liposomes)" see the whole document see page 5553; table 1</p> <p>---</p>	1-4, 6, 10-12
Y	<p>SCIENCE, vol. 261, no. 5124, 20 August 1993, WASHINGTON (US), pages 1004-1012, XP002027216</p> <p>C.A. STEIN ET AL. : "antisense oligonucleotides as therapeutic agents-is the bullet really magical" see page 1005, column 1; figure 1</p> <p>-----</p>	1-4, 6, 10-12

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 96/14146

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claim(s) 10
is(are) directed to a method of treatment of the human/animal
body, the search has been carried out and based on the alleged
effects of the compound/composition.
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such
an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all
searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment
of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report
covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is
restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.
 No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 96/14146

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
DE 4110085 A	01-10-92	NONE		
WO 9503788 A	09-02-95	US 5417978 A	23-05-95	
		AU 7407994 A	28-02-95	
		CA 2168243 A	09-02-95	
		EP 0711149 A	15-05-96	
		JP 9501160 T	04-02-97	